REMARKS

Claims 11-29 have been withdrawn from consideration as being non-elected and have been cancelled. Applicant points out that a typographic error was made in the Applicant's Response of October 1, 2002, i.e., Group II should refer to claims 11-29, not to claims 11-20.

New claims 30-38 have been added. Support for new claims 30-38 is found in original claims 1-10 of the present application and the description at p. 4, lines 26 -28 and p. 5, lines 4 to 6 of the present specification

I. 35 USC § 112

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The Examiner states that the recitation of particle sizes in terms of percentages in the instant claims is vague and confusing, because from the limitation "less than about 30% by weight of the particles exhibit a particle size of greater than about 425 micrometer" it appears that the particles in the size range of greater than 425 microns is not essential for the composition, and from the limitation "greater than about 80% by weight of the particles exhibit a particle size of greater than about 45 micrometer" includes any size above 45 microns i.e., even 425 microns. The Examiner concludes that it is unclear from the claim expression as what particle sizes are being claimed by Applicant's and has requested clarification.

Applicant agrees that, when considered separately, each of the Examiner's comments regarding the claim limitations is correct, i.e., the limitation of Applicant's claim 1 requiring "less than about 30% by weight of the particles exhibit a particle size of greater than about 425 micrometer" it does not require that the claimed composition actually

contain any particles in the size range of greater than 425 microns, and the limitation Applicant's claim 1 requiring "greater than about 80% by weight of the particles exhibit a particle size of greater than about 45 micrometer" includes any size above 45 microns, but disagrees that this renders the claim unclear. Applicant submits that, taken in combination, the limitations effectively require that at least 50 (i.e., 80 - 30) % by weight of the particles exhibit a particle size of from greater than 45 microns to 425 microns.

For the reasons discussed above, Applicant submits that claims 1-10 of the present Application are not indefinite and Applicant therefore requests that the Examiner reconsider and withdraw the rejection of claims 1-10 of the present application under 35 U.S.C. 112, second paragraph.

II. 35 USC § 102

Claim 1 stand rejected under 35 U.S.C. 102(b) as being anticipated by US 4,711,774 ("Denick").

The Examiner correctly states that claim 1 of the present application is directed to a composition comprising guaifenesin and a binder and being in the form of particles, wherein less than about 30% by weight of the particles are greater than 425 micrometers in size and greater than about 80% by weight of particles are greater than about 45 micrometers.

The Examiner further states that Denick discloses compositions containing guaifenesin mixed with magnesium aluminum silicate until a homogenous mixture is obtained (see example 1, in col. 11, lines 20-43) and that magnesium aluminum silicate is used as an adsorbate for guaifenesin. The Examiner asserts that although Denick does not call it binder, the magnesium aluminum silicate of Denick "reads on instant binder" because the term is broad and does define any specific compound. The Examiner further states that Denick discloses that the composition is dried and milled to produce a free flowing particulate material having a particle size of about 100 microns and that instant

claim 1 states less than 30% particles have a size greater than 425 microns, which includes 0%-30%. In other words, particles >425 microns are not required for the composition. The Examiner concludes that the composition of Denick anticipates instant composition of claim 1.

Denick discloses a medicament adsorbate, wherein a solution of a medicament, such as, e.g., guaifenesin, is sorbed in a magnesium aluminum silicate adsorbent (col.1, line 54 to col. 2, line 8 and Example 1 of Denick). Denick does not indicate that any such adsorbate, including the particulate guaifenesin adsorbate of Example 1 of Denick is, by itself, compressible into a compressed dosage form. To the contrary, Denick discloses that sugars and excipients (such as, e.g., a "binder") are generally added to the particulate adsorbate of Denick, as separate components, in order to make compressed dosage forms, such as, e.g., compressed tablet lozenges (see col. 6, lines 4-9 of Denick).

The specification of the present application indicates that guaifenesin itself is generally regarded as being non-compressible and therefore not readily amenable to production of directly compressible granualtions (see page 1, lines 28-30 of the present application), and any pharmaceutically acceptable compound capable of rendering the guaifenesin compactable is suitable as the binder compound of Applicant's claimed composition (see page 5, lines 28-30 of the present application).

Applicant submits that the disclosure of Denick does not anticipate the composition of Applicant's claim 1 because the disclosure of Denick does not satisfy the limitation of Applicant's claim 1 requiring a particulate guaifenesin composition comprising guaifenesin and binder, i.e., when properly interpreted in light of the description set forth in the present specification, the term "binder" in Applicant's claim 1 does not read on the magnesium aluminum silicate of Denick. Denick provides no disclosure of suggestion that the guaifenesin/magnesium aluminum silicate composition of Denick is compactable or that the magnesium aluminum silicate component of Denick would in any way render guaifenesin particles compactable. To the contrary, the magnesium aluminum silicate component of Denick performs an entirely different function than the binder component of

Applicant's claimed composition, i.e., the magnesium aluminum silicate component of Denick acts as an adsorbent for a liquid guaifenesin solution (see col. 1, lines 54-59 of Denick).

Applicant submits Applicant's claims 4, 9 and 10 further distinguish over Denick by requiring by requiring that the claimed composition comprises from about 85 to about 97.5 percent by weight guaifenesin. Denick discloses compositions which apparently comprise, at most, about 18.4% percent by weight guaifenesin (i.e., 260 g guaifenesin/(1200 magnesium aluminum silicate +260 g guaifenesin), see Example 1 of Denick). Applicant submits that Denick does not disclose compositions comprising a relative amount of guaifenesin that satisfies the limitations of Applicant's claims 4, 9 and 10.

For the reasons discussed above, Applicant submits that Applicant's claim 1 is not anticipated by the disclosure of Denick and therefore requests that the Examiner reconsider and withdraw the rejection of Applicant's claim 1 under 34 USC 102(b) as being anticipated by Denick.

III. 35 USC § 103

(a) 35 USC § 103/Denick et al

Claims 5-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Denick.

The Examiner states that Denick teaches a particulate composition comprising guaifenesin and magnesium aluminum silicate and that Denick teaches in Example 1 a composition that , upon milling to a free flowing composition, has a particle size about 100 microns. The Examiner further states that Denick suggests that the particulate size ranging from 10 to 150 microns is suitable for the invention and that, for the reason discussed in the rejection under 35 USC 102(b), the magnesium aluminum silicate of

Denick "reads on instant binder". The Examiner acknowledges that Denick differs from the instant claims in the percentages of particle sizes, but concludes that it would be obvious for one of an ordinary skill in the art at the time of the instant invention to choose and obtain guaifenesin composition having claimed particle sizes because Denick teaches that suitable particle sizes in the range of 10-150 microns are preferred for adsorbing sufficient quantities of medicament solution to prepare an acceptable drug product.

The Examiner acknowledges that Denick does not state the flow rate recited in claim 8, but concludes that because Denick teaches particles in the same size range as required by the claims, optimizing the flow rate to produce a free flowing particulate formulation, having the claimed flow rate would have been obvious for a skilled artisan at the time of the instant invention.

Applicant submits that, for the reasons discussed above in regard to the rejection under 35 USC 102(b), the disclosure of Denick is deficient with respect to the claimed binder component of Applicant's particulate guaifenesin composition and further submits that the Examiner's arguments do not remedy this deficiency.

Applicant submits that the Examiner's arguments regarding particle size and flow rate are not relevant to Applicant's claimed composition, since the composition of Denick's adsorbate particles is different from the composition of Applicant's claimed particles. Applicant further submits that the reference in claim 1 of Denick to adsorbate particle size of 100 microns can only reasonably be interpreted as an average particle size, which does not characterize the particle size distribution of Denick's adsorbate, and that therefore Denick does not disclose a particulate having a particle size distribution that satisfies Applicant's claimed particle size distribution.

Applicant submits that one having ordinary skill would not have found Applicant's claimed invention obvious in view of Denick, since the adsorbate particles of Denick fail to satisfy the limitation of Applicant's claim 1 requiring a binder, the adsorbate particles of

Denick fail to satisfy Applicant's claimed particle size distribution, and neither the disclosure of Denick nor the Examiner's arguments has remedied these deficiencies.

Applicant submits Applicant's claims 4, 9 and 10 further distinguish over Denick by requiring by requiring that the claimed composition comprises from about 85 to about 97.5 percent by weight guaifenesin. As discussed above, Denick discloses compositions which apparently comprise, at most, about 18.4% percent by weight guaifenesin. Applicant submits that Denick does not disclose or suggest compositions comprising a relative amount of guaifenesin that satisfies the limitations of Applicant's claims 4, 9 and 10.

For the reasons discussed above, Applicant submits that the subject matter of Applicant's invention would not have obvious at the time of the invention was made to a person having ordinary skill in the art in view of the disclosure of Denick and therefore request that the Examiner reconsider and withdraw the rejection of claims 5-8 under 35 U.S.C. 103(a) as being unpatentable over Denick.

(b) 35 USC § 103/Blume et al

Claims 1-10 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,372,252 to Blume et al ("Blume").

The Examiner states that Blume teaches sustained release formulations comprising guaifenesin, a hydrophilic polymer such as hydroxypropyl methylcellulose, a water insoluble polymer and other tabletting ingredients (col. 4, lines 4-28 and col. 6, lines 1-43), and that among the pharmaceutical additives, Blume teaches lubricants such as magnesium stearate, calcium stearate etc; binders such as povidone (polyvinylpyrrolidone), gelatin, starch; glidants such as talc or silicon dioxide, stabilizers and other excipients such as lactose, sorbitol etc (col. 6, lines 45-65). The Examiner further states that Blume teaches preparing the composition by granulation and compression (col. 8), which includes as one of the steps, drying and milling the

composition and passing through sieves of 100 mesh screen size (col. 8, lines 20-25). The Examiner notes that a 100-mesh size screen allows for particles of 150-micron size (see instant description on page 14) and urges that Blume therefore suggests preparing particles in the similar size ranges as that of the instant invention. The Examiner acknowledges that Blume does not teach the exact percentages of the particle sizes as claimed by Applicant, but concludes that optimizing the particle sizes of guaifenesin comprising medicament formulation depending on the type of preparation, i.e., compression tablet (col. 8) or a capsule (col. 9), would have been obvious for one of an ordinary skill in the art.

As acknowledged by the Examiner, Blume does not disclose a guaifenesin composition having Applicant's claimed particle size distribution. Applicant further submits that, contrary to the assertion of the Examiner, Blume does not suggest preparing particles in the similar size ranges as that of Applicant's invention, i.e., the particle size range claimed by Applicant is much narrower and, as claimed in Applicant's claims 5, 6, 7, 9 and 10, is skewed toward smaller size particles than the particle size distribution disclosed by Blume. Blume discloses that "not more than about 30% of the resulting granulation comes through a 100 mesh screen and that not more than about 10% of the resulting granulation is retained on a 10 mesh screen" (see col. 8, lines 19-23 of Blume), i.e., that at least 60% of the granulation has a particle size of greater than 150 micrometers , i.e., the size of the openings in a 100 mesh screen, and less than 200 micrometers, i.e., the size of the openings in a 10 mesh screen. As discussed above in regard to the rejection under 35 USC 112, the particles of Applicant's claimed composition have a particle size distribution wherein less than about 30% by weight of the particles exhibit a particle size of greater than about 425 micrometer and greater than about 80% by weight of the particles exhibit a particle size of greater than about 45 micrometer, i.e., wherein at least 50% by weight of the particles exhibit a particle size of from greater than 45 microns to 425 microns. Applicant's claims 5, 6, 7, 9 and 10 require the presence of particles (from about 10 to about 60 percent by weight (claims 5, 6, and 9) or from about 17 to about 55 percent by weight (claims 7 and 10)) having a particle

size of from greater than 45 micrometers to less than 150 micrometers, i.e., particles that fall through a 100 mesh screen.

Applicant acknowledges that Blume discloses that the "GUAIFENESIN DC" composition of Blume can, in combination with other ingredients (see col. 8, lines 31-34 of Blume), be compressed to make, e.g., tablets (see col. 8, lines 35-42 of Blume), but submits that Blume shows no recognition of the problems addressed by Applicant's invention, i.e., the need for a guaifenesin composition that offers both improved flow properties and improved robustness with regard to compression processing conditions (see page 2, lines 16-25 of the present application).

Applicant submits that the subject matter of Applicant's invention would not have obvious for one of an ordinary skill in the art at the time of the invention was made because Blume does not disclose or suggest the claimed particle size distribution of Applicant's composition, Blume does not recognize the problems addressed by Applicant's invention, that lacking any recognition of such problems, Blume provides no motivation for seeking to further optimize the particle size distribution of the direct compressed guaifenesin composition of Blume, and, even if it were obvious to try to further optimize Blume's particle size distribution, nothing in Blume would have led one to the particle size distribution claimed by Applicant.

For the reasons discussed above, Applicant submits that the subject matter of Applicant's invention would not have obvious at the time of the invention was made to a person having ordinary skill in the art in view of the disclosure of Blume and therefore request that the Examiner reconsider and withdraw the rejection of claims 5-8 under 35 U.S.C. 103(a) as being unpatentable over Blume.

IV New Claims 30-38

New claims 30 and 32 each further distinguish the invention of Applicant's claim 1 over Denick by requiring that the claimed composition comprise an amount of guaifenesin

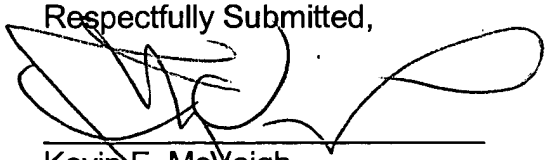
within a defined range. As discussed above, Denick discloses compositions which apparently comprise, at most, 18.4% percent by weight guaifenesin. Applicant submits that Denick does not disclose or suggest compositions comprising an amount of guaifenesin that satisfies the limitations of new claims 30 and 32.

New claims 31, 37 and 38 each distinguish Applicant's invention over the references relied on by the Examiner for the reasons discussed above in regard to claims 1, 9 and 10 of the present application and each further distinguish Applicant's invention over those references by requiring that the claimed composition be capable of being compressed into a compressed dosage form without addition of other components. As discussed above, the guaifenesin-containing particles of Denick and Blume are each blended with other components prior to compression in order to make a compressed dosage form. Applicant submits that neither Denick nor Blume disclose or suggest compositions that satisfy the particle size distributions required by claims 37, 36 and 37 and are capable of being compressed into a compressed dosage form without the addition of other components as required by Applicant's claims 31, 37 and 38.

V Conclusion and Request for Allowance

For all the reasons discussed above, Applicant submits that all claimed pending in the present application are in condition for allowance and now requests that the Examiner issue a *Notice of Allowance* for claims 1- 10 and 30-38 in the present Application.

Respectfully Submitted,



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